Neovascularization: An “innocent bystander” in recurrent varicose veins

Bridget Egan, FRCSI, Michael Donnelly, AFRCSI, Mary Bresnihan, AFRCSI, Sean Tierney, FRCSI, and Martin Feeley, FRCSI, Dublin, Ireland

Objective: Varicose vein recurrence after surgery occurs in up to 60% of patients. A variety of technical factors have been implicated, but biological factors such as neovascularization have more recently been proposed. The objective of this study was to characterize the relative contribution of technical and biological factors to recurrence in a large prospective series of recurrent varicose veins.

Methods: Duplex and operative findings were recorded prospectively in a consecutive series of 500 limbs undergoing surgery for recurrent varicose veins between 1995 and 2005 in a university teaching hospital. Only limbs with previous saphenofemoral junction surgery were included. All limbs had preoperative duplex mapping by an accredited vascular technician who assessed the status of the great saphenous vein (GSV) in the thigh and groin, sought sonographic evidence of neovascularization, and reported on the presence of reflux in the short saphenous vein and perforator sites (typical and atypical). All operations were performed with an attending vascular surgeon as the lead operator.

Results: Primary GSV surgery was incomplete in 83.2% of limbs. A completely intact GSV system was present in 17.4% of limbs. An incompetent thigh saphenous vein was present in 44.2% of limbs, 37.6% had GSV stump incompetence with one or more intact tributaries, and 16% had both a residual thigh GSV and an incompetent stump with intact tributaries. Non-GSV sites of reflux were identified in 25% of limbs. Neovascularization was identified on duplex scanning in 41 (8.2%) limbs. However, in 27 of these, surgical exploration revealed a residual GSV stump with 1 or more significant tributaries. Each of the remaining 14 (2.8%) limbs had a residual incompetent thigh GSV.

Conclusions: Despite reports to the contrary, neovascularization occurs in a relatively small proportion of patients with recurrent varicose veins. All recurrent varicose veins associated with duplex-diagnosed neovascularization are also associated with persistent reflux in the GSV stump tributaries, thigh GSV, or both. Recurrence after primary varicose vein surgery is associated with inadequate primary surgery or progression of disease, and neovascularization alone is not a cause of recurrent varicose veins. (J Vasc Surg 2006;44:1279-84.)

Venous disease, including varicose veins, is one of the most commonly reported chronic medical conditions and a substantial source of morbidity in the United States. Estimates of the prevalence vary widely from 12% to 40% in men and 25% to 73% in women.

In the United Kingdom, almost 90,000 operations are performed per year. Recurrence rates of 20% are common, with rates as high as 70% at 10 years reported. Up to 25% of procedures for varicose veins are performed for recurrent disease, thus placing considerable demands on health care resources. It is important to note that recurrent varicose vein (RVV) surgery carries a much greater morbidity risk to the patient than primary surgery.

Varicose vein recurrence after primary surgery has been attributed to several etiologic factors, the main ones being incomplete initial assessment, inadequate primary surgery, neovascularization at a previously ligated saphenofemoral junction (SFJ), and disease progression due to the development of new incompetent sites. A multicenter study from Italy in 194 patients reported recurrence due to technical error in 78.7%, diagnostic error in 9.2%, and unidentifiable causes in 12%.

The objective of this study was to identify the site(s) of venous reflux causing RVVs after surgery in a large representative series of patients undergoing surgery for RVV. Furthermore, drawing on the knowledge of the widely varied anatomy of the saphenofemoral complex gained from a study of a cohort of 2089 patients undergoing primary varicose vein surgery, the study then sought to identify a possible relationship between anatomic variation of the great saphenous vein (GSV) and inadequate primary GSV surgery.

PAIRED METHODS

All patients undergoing surgery for the treatment of RVVs between January 1995 and August 2005 were included. Only patients with previous surgery to the SFJ, as evidenced by skin and perijunctional scarring, were included in this study. Patients with RVVs who did not previously undergo SFJ surgery were excluded. The previous operations were performed over a wide time period in many institutions, and operation records were not available.

All limbs had preoperative venous duplex ultrasound scanning performed by an experienced accredited vascular technician. Patients were scanned by using a 7.5-mHz...
transducer in B mode. The purpose of the scan was to assess
and map the residual GSV anatomy. Specifically, record was
made of the status of the SFJ, residual thigh GSV, and
continuity between the stump and GSV. All superficial
venous tributaries were examined to determine, if possible,
their filling sources, including the medial knee perforating
vein and anomalous perforators. The status of the saphe-
nopopliteal junction and calf perforators was also deter-
mined. Reflux was defined as the reverse of flow lasting
more than 1 second. Neovascularization was identified by
the presence of refluxing tortuous vessels arising from the
area of the SFJ.

The surgical procedure was dictated by the findings of
the ultrasound examination. Patients who, on ultrasound
scanning, had an intact GSV system, a residual stump, or
neovascularization underwent groin re-exploration. All op-
erations were performed by a consultant vascular surgeon as
the principal operator. The femoral vein was identified at
the inguinal ligament and dissected distally until the infe-
rior limit of the SFJ was identified. Tributaries to the
junction were clipped and divided. The GSV was transfix-
ed, ligated, and divided within 1 cm of the junction with the
femoral vein. To ensure that all feeding tributaries were
identified, the femoral vein was dissected to 2 cm distal to
the SFJ. All SFJs reported on preoperative duplex scanning
to have neovascularization were explored, and the junction
was transfixed and divided. Where the GSV had been
ligated in the groin but a patent and incompetent GSV
remained in the thigh, it was isolated just below the knee,
either directly or via a tributary, and a vein stripper was
passed toward the groin to facilitate isolation and stripping
of the vein via a groin wound. Stripping of the great
saphenous was considered adequate to deal with incompe-
tent medial knee perforators. All other incompetent thigh
perforators were marked before surgery and were ligated
and divided through a small overlying incision.

Patients with saphenopopliteal incompetence had pre-
operative marking of the junction. The short saphenous
vein was transfixed, and the terminal 5 cm of the short
saphenous vein was excised. When reported as being in-
competent, the cranial extensions of the short saphenous
vein and/or gastrocnemius vein were dissected, divided,
and ligated. In two limbs, the cranial extension of the short
saphenous vein was stripped to the groin by using a vein
stripper.

On completion of the surgical procedure, operative
findings were recorded diagrammatically. The data were
then entered into an Excel (Microsoft, Dublin, Ireland)
spreadsheet for analysis.

RESULTS

During the study period, 500 consecutive operative
procedures were performed for RVV. Seventy-eight per-
cent of the patients were women, with a mean (SD) age of
50.0 years (10.6 years); the mean (SD) age of the men was
57.9 years (4.5 years).

Four hundred sixteen limbs (83.2%) had varicosities
associated with reflux in the great saphenous system. An
intact great saphenous system was present in 87 (17.4%) lim-
bgs (Fig 1). Sixteen of these patients also had saphenopo-
pliteal incompetence, and one patient had an incompetent
calf perforator. A residual GSV stump with intact tributaries
was present in 188 (37.6%) limbs (Fig 2) and was the only
source of reflux in 100 limbs. An incompetent thigh GSV
was identified in 221 (44.2%) limbs (Fig 3) and was the only
source of reflux identified in 104 limbs. Twenty-one (4.2%)
also had saphenopopliteal incompetence. In 80 (16%)
limbs, varicosities were associated with a combination of a
residual GSV stump with tributaries and persistent incom-
petent thigh GSV (Fig 4). The GSV communicated with an
incompetent medial knee perforating vein in 12 limbs.

Neovascularization, as evidenced by the presence of reflux-
ing tortuous vessels arising from the area of the SFJ, was
identified by duplex scan in 41 limbs (8.2%).

At surgery, all had a mass of fibrous scar tissue
involving the previously sectioned end of the GSV.
Twenty-seven of these had significant saphenous stump
tributaries. Each of the remaining 14 (2.8%) limbs also had
an incompetent thigh GSV. No limb had RVVs associated
with neovascularization alone.

A total of 114 limbs (22.8%) had saphenopopliteal
incompetence, in 65 of which it was the sole source of
reflux. In two of these limbs, the reflux was from the vein of
Giacomini, and in these patients the vein was stripped from
the thigh. Only 84 (16.8%) limbs presenting with varicose
vein recurrence had no element of residual GSV reflux.
Seven limbs had varices that were associated with reflux in
cross-groin/pelvic/vulval veins, in four of which they were
the only source of reflux. In two they were associated with
a residual thigh GSV, and in one, with a persistent incom-
petent saphenous stump and residual GSV. Atypical thigh
perforators alone were the only sites of reflux identified in
four limbs. In 12 limbs, no reflux site was identified, and
these were treated by multiple avulsions.

DISCUSSION

Varicose vein recurrence after surgery is an all-too-
frequent phenomenon, the treatment of which places a
significant burden on health care systems and resources. It is
evident that every effort should be made to reduce the
recurrence rate if possible, not just to save valuable re-
sources, but to avoid the more difficult and proportionally
dangerous redo surgery.7 This study, which included only
patients who had previously undergone groin dissection, is
the largest of its kind to date, to our knowledge.

Of the 500 people who had previous GSV surgery, 416
(83.2%) required further surgery in the GSV system to deal
with their varicose veins. Duplex and operative studies from
the Western world report recurrent SFJ incompetence in
84% to 99% of cases.9,14,15 There are three indications for
exploring the SFJ at RVV surgery: a completely intact but
incompetent GSV system, a great saphenous stump with
intact tributaries, and neovascularization.

The finding that almost one fifth of limbs (n = 87;
17.4%) still had an intact GSV system is alarming. However,
previous operative studies of 619 and 7116 limbs reported
intact GSV systems in 50.8% and 57%, respectively. Imaging
studies also reported similar rates of intact GSV sys-
tems.17 Apart from hemorrhage necessitating abandon-
ment of the procedure, failure to ligate and divide the SFJ
can be explained on the basis of anatomic variation. A large
lateral thigh tributary or lateral element of a bifid system
can easily lead to misinterpretation of the anatomy: the
lateral vein is mistaken as the GSV and the medial vein as
the femoral and are treated as such, thus leaving the long
saphenous complex intact. The lateral thigh tributary may
be substantial in size and is not infrequently the major
filling source for the varicosities. This vein is referred to as
the lateral accessory vein or anterolateral tributary, and its
importance in varicose vein disease has been highlighted by
several authors in recent years.6,18,21 A bifid GSV was
reported to occur in 378 (18.1%) of 2089 limbs undergo-
ing primary varicose vein surgery.10

Its recognition is rendered much more difficult by the
presence of an aberrant pudendal artery traversing behind a
large ascending tributary and anterior to the GSV (or
between the two trunks of a bifid GSV system), thus
resulting in an appearance identical to the “normal” junc-
tion, a variation that occurs in 4.6% of dissections.13 A

Fig 2. Residual long saphenous vein stump incompetence.

thorough appreciation of the anatomic variation and ade-
quate visualization of the femoral vein may reduce the risk
of this error.

Failure to remove the ligated GSV from the thigh has
previously been shown to be associated with high recur-
rence rates.10,22 In this study, the GSV had been divided
but not stripped from the thigh in 221 (44.2%) limbs, in
more than half of which (120 limbs) it was the only iden-
ifiable cause of recurrence. This is in keeping with the
findings of Dwerryhouse et al23 and Winterborn et al,24
who reported that stripping the thigh GSV reduced recur-
rence rates by 66% at 5 years after the primary varicose vein
surgery. Stripping of a GSV does not, however, guarantee
complete thigh GSV obliteration. In the thigh, up to 24%
of GSV systems are bifid.25 When a true bifid system is
identified, the vein stripper can be passed from the SFJ
down both veins, thus avoiding a persistent thigh GSV.
However, when the vein bifurcates distal to the operative
field, the bifid nature of the vein may not be evident, and
one vein limb may be left in situ, a scenario that can be
avoided only by preoperative imaging and GSV mapping.
Intraoperative ultrasonography may also be of benefit.

Stripping the GSV from the thigh should also reduce recurrences associated with an incompetent medial knee perforator. In all but 1 of 11 limbs with an incompetent thigh perforator, it communicated directly with a residual thigh GSV. As with the GSV, stripping does not guarantee disruption of the medial knee perforating vein, because the stripper can pass to a large superficial tributary in the lower third of the thigh. This probably explains the small number of cases in which a portion of patent GSV was identified in only the lower half of the thigh.

In 188 (37.6%) limbs, recurrence was associated with a
residual incompetent GSV stump with intact tributaries, a
figure similar to previous reports of 44.2%9 and 44%.16
with neovascularization on ultrasonography, surgical exploration revealed a GSV stump with 1 or more significant tributaries. Each of the remaining 14 (2.8%) limbs had a residual incompetent thigh GSV.

These findings are similar to those of Viani et al and Turton et al, who found recurrence related to neovascularization in only 3.2% and 4%, respectively, but they are at variance with recent literature in which this phenomenon is reported to be partly or wholly responsible for up to 94% of recurrences. This apparently irrefutable discrepancy is probably explained by different interpretations of the term neovascularization. In this study, all veins joining the GSV stump or junctional area were deemed missed tributaries, whereas in other studies stump tributaries as substantial as 3 mm in diameter have been attributed to neovascularization. As seen previously, stump tributaries were present in 37.6% of limbs, which is quite similar to the rates of neovascularization reported in other studies. Virtually all studies that report a high incidence of neovascularization-related recurrences are based solely on imaging without the benefit of operative corroborations. Our findings strongly support the theory of El Wajeh et al that saphenofemoral venous channels associated with RVVs are not neovascular but represent adaptive dilation of pre-existing venous channels in response to abnormal hemodynamic forces.

Advocates of endovenous GSV ablation have proposed that avoiding a groin incision and dissecting the SFJ will avert neovascularization, thus preventing a significant source of recurrence. The Closure registry reported ultrasound evidence of neovascularization in only 0.1% of limbs after endovascular radiofrequency ablation over a 5-year follow-up. It is interesting to note that Labropoulos et al reported neovascularization in 5% after endovenous laser or radiofrequency GSV ablation procedures. Although the numbers are small, this further supports the theory that persistent venous tributaries to the GSV are being erroneously classified as neovascularization on ultrasonography. This body of evidence supports the belief that failure to disrupt the tributaries to the terminal GSV may significantly increase the risk of varicose vein recurrence. Although it is tempting to speculate that endovenous therapies will be associated with high recurrence rates secondary to residual groin tributaries, this can be established only by long-term systematic duplex follow-up.

Fifty-two (10.4%) limbs deemed to have had inadequate primary surgery also had incompetence at other sites. Forty-nine (9.8%) limbs had saphenopopliteal incompetence, 3 (0.6%) of which also had calf perforator incompetence and 11 (3.1%) of which had thigh perforator incompetence. Because of the nature of the study population, it is impossible to know whether these incompetent sites were present at the time of the original operation. Similarly, it is impossible to know whether the 49 patients with saphenopopliteal incompetence and the 5 limbs with atypical thigh perforator incompetence alone, without GSV incompetence, had these sources of reflux at the time of the primary operation.
In only seven (1.4%) limbs were cross-groin or -valvular veins thought to be the major source of venous filling. This cause of recurrence, not mentioned in most studies, is regarded as a minor factor in recurrence,9 but in one study cross-groin collaterals were found in 7 of 28 groin explorations.10 Division of the SFJ tributaries proximal to coalescence with other tributaries might help avoid this small recurrence potential. No limb had recurrent varices due solely to calf perforator incompetence, and perforator disruption was performed in less than 1%. Even though high rates of calf perforator incompetence are found in limbs with RVV, rarely are they believed to be primarily or solely responsible for the recurrences.15,25

In this operative and duplex ultrasonographic study of 500 RVVs, 83.2% of recurrences were associated with incomplete GSV surgery. The findings emphasize the importance of completely dissecting the SFJ, ligating and dividing tributaries to the level of secondary tributaries, where possible, and ligating the GSV flush with the femoral vein. The importance of stripping the GSV is once again evident. A thorough understanding of the highly variable GSV anatomy is essential to avoid inadequate primary surgery.

We believe that this study confirms that neovascularization, although not an uncommon duplex ultrasonographic finding, is rarely the sole cause of RVVs. We conclude that the vast majority of RVVs are associated with incomplete primary surgery and may be avoidable.26,37

AUTHOR CONTRIBUTIONS
Conception and design: MF
Data collection: MD, MB, MF
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Critical revision of the article: ST
Final approval of the article: MF
Overall responsibility: MF

REFERENCES
DISCUSSION

Dr Thomas O’Donnell (Boston, Mass). Your interesting presentation raises several questions. First of all, who performed the original surgery? Were the procedures done on your unit, and, if not, did you have access to the case notes in order to determine the experience level of the initial surgeon registrar, junior registrar, or consultant? Since your presentation suggests that many of the recurrences may be due to technical causes, the level of experience of the operating surgeon would be an important factor in avoiding technical causes of recurrence.

My second question is directed toward the use of preoperative diagnostic duplex studies. In the UK and Ireland, I gather, routine duplex exams of patients prior to varicose vein surgery is not the norm. By contrast, in the United States, for several reasons, particularly due to insurance requirements for documentation of reflux, patients undergo preop duplex studies. As a result, the surgeon might be aware of anatomical abnormalities such as a duplicated great saphenous, which could lead to “recurrence.”

Finally, most of us in the United States have shifted to an endovenous ablation technique for saphenous reflux, so that your series on recurrences following the “open” technique may be an interesting benchmark against which to compare the causes of recurrence following endovenous ablation. In addition, we have used endovenous ablation to manage reoccurrence after “open” surgery.

Thank you for your stimulating presentation.

Dr Feeley. The primary operations were carried out in a large number of institutions by a large number of surgeons. No, it wasn’t possible to get these data. The results are totally in keeping with all other reports, surgical series, of recurrent varicose veins and their causes.

I think the data here are not of historical interest; I think they are extremely relevant and important in relation to the newer treatment modalities. The finding that 20% of patients had a stump before we find out the real value of endovenous therapies. The question is, how long it is necessary to wait to see if this is the most frequent cause of recurrence following endovenous ablation. In Van Rij’s paper, a histologic evaluation was performed to distinguish between residual normal venous tributaries and immature vessels of neovascularization. So I’m wondering if you have done any histologic study to provide evidence that those vessels that caused recurrence were indeed residual mature vessels and not neovascularizations.

Dr Feeley. Yes, certainly, if one is to read the literature, the importance of neovascularization is very evident. However, the vast majority of these studies are based on imaging only. There is no surgical corroboration of the duplex findings. I would suggest to you that duplex findings are images and their interpretation is what’s important. I suggest that these series of duplex neovascularizations are in fact GSV stump tributaries.

The second question was histology. Yes, I agree that this would be very nice, and it has been done by others, including Jonathan Earnshaw, and they have shown neovascularization.

First, I didn’t do it, not because I’m lazy, but may be a coward. I think exciting tissue from the groin of a patient out of curiosity with the possible result of limb edema is not justifiable. I am not denying that new vessels grow in scar and healing tissue; I’m not arguing with that at all. There is no doubt that it does happen. What I am saying is that it is not an important factor in the etiology of recurrent varicose veins.

Dr Charles Brantigan (Denver, Colo). I would like to put you on the spot and ask how your work relates to endovenous ablation of varicose veins.

The endovenous ablation techniques are not able to deal with those branches that you’ve described at the saphenofemoral junction, and, in fact, there have been publications suggesting that it’s best to leave those branches intact.

How does the work that you’re reporting today relate to the new techniques in endovenous therapy? On the basis of your data, what do you expect the long-term results of these procedures to be?

Dr Feeley. Well, first, there have been reports, even at this early stage, of neovascularization following the endovenous ablation techniques. The retention of the junctional branches, as we call them, is believed to be important. I have just shown you that these junctional branches with the retained stump, in this study, were present in 37.6% of recurrences and were the only source of reflux in 20%.

I should point out that the debate really is whether these tributaries to which I refer are in fact newly developed vessels, what you call neovascularization, or whether they are, in fact, retained missed tributaries. These tributaries were identical to those which I saw and described in an anatomic study I did in parallel with this, in which I dissected 2089 groins, and furthermore over 33% had what I call junctional branches—in other words, joined at the saphenofemoral junction line or deep to the fascia.

Dr Harry Schanzer (New York, NY). I enjoyed your paper very much. It is very provocative, when considering the new endovenous techniques.

My question is directed to what just was discussed. In the endovenous techniques, one deliberately does the equivalent of a low saphenous ligation, leaving the most proximal tributaries subjected to reflux from the incompetent saphenofemoral valve. The question is, how long is it necessary to wait to see if this potential reflux produces recurrences? In your study, what was the time frame between surgery and the onset of recurrence?

Dr Feeley. Yes, I agree, we have to wait for a number of years before we find out the real value of endovenous therapies. It would be interesting to know, and unfortunately I don’t know the answer to your question. They were over a wide range of time and, indeed, most patients can’t remember exactly when they had their surgery.